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AWARD NUMBER: W81XWH-15-1-0684

TITLE: Diagnosis of Late-Stage, Early-Onset, Small-Fiber Polyneuropathy

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PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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Approved for Public Release
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13. SUPPLEMENTARY NOTES

14. ABSTRACT
As our research team has not been granted DoD HRPO approval, no subject research has taken place. Therefore, we are unable to provide any significant finding during this research period.

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
U					USAMRMC
a. REPORT	b. ABSTRACT	c. THIS PAGE	UU	13	19b. TELEPHONE NUMBER *(include area code)*

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1. INTRODUCTION: Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

Gulf War Veterans report chronic multi-symptoms similar to that found in the treatable nerve disease small-fiber polyneuropathy (SFPN). Dr. Oaklander's preliminary evidence showed 47% of Gulf War Veterans had results consistent with SFPN. Evaluation for SFPN is expensive and lengthy. The aim of this research is to 1) develop screening tools for simple diagnosis by using patient-report symptom questionnaire and standardized medical exams, 2) develop biotechnology tools for simple diagnosis (sweat testing and pupilometry), 3) identify gene polymorphisms to detect risk for SFPN.

2. KEYWORDS: Provide a brief list of keywords (limit to 20 words).

None to report

3. ACCOMPLISHMENTS: The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Goal 1) Human Research Approval
Subtasks:
a) Develop protocol, obtain IRB and Human Research Protection Office approvals (Oct 2015 – Dec 2015) - **75% completed**

Goal 2) Recruitment
Subtasks:
a) Search existing veterans database, outreach to new veteran patients, advertisement at VA facilities, contact with VSOs, search of 30,000 veteran epidemiological study database, leverage other ongoing studies
(Dec 2015 – Mar 2018)

Goal 3) Specific Aim 1: To develop and evaluate screening tools for diagnosis and monitoring of longstanding eoSFPN, specifically a patient-reported symptom questionnaire and a standardized examination for medical personnel.
Subtasks:
a) Administer/validate questionnaires/forms (Sept 2016- Mar 2018)
b) Data analysis and develop publications (Mar 2018 – Sept 2018)

Goal 4) Specific Aim 2: To develop and evaluate simple biotechnology devices for diagnosing and monitoring longstanding eoSFPN based on detection of abnormal sweating and pupil size and reactivity.

Subtasks:

a) Obtain supplies (instruments, fixative, mailers) for skin biopsy (Oct - Dec 2015) **- completed**

b) Study veterans with AFT and skin biopsy (May 2016 – Mar 2018) **0% completed**

c) Perform Sudoscan and pupillometry (May 2016 – Mar 2018) **0% completed**

d) Data analysis to determine sensitivity/specificity of Sudoscan and pupillometry (Sept 2016 – May 2018)

e) Publication of Sudoscan and pupillometry findings (Mar 2018 – Sept 2018)

Goal 5) Specific Aim 3: To develop and evaluate tools for identifying gene polymorphisms that convey risk for eoSFPN

Subtasks:

a) Blood draw for genetic material (Dec 2015 – Sept 2017)

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

1. Major Activities:

a) VANJ IRB approval for study including Research Monitor granted on Sept 1, 2016.

b) VANJ IRB documents submitted for HRPO approval on Sept 2, 2016.

2. Specific Objectives within this quarter

a) Obtain IRB and Human Research Protection Office approvals
b) Begin AFT, skin biopsy, sudoscan, and pupillometry testing
c) Begin collecting blood for genetic material

3. Significant Results of Key Outcomes

a) VANJ IRB approval was granted on March 30, 2016 and included a Research Monitor on Sept 1, 2016.
b) Testing has not begun due to not having an approved HRPO protocol
c) Collection of blood (and enrollment) has not begun due to not having an approved HRPO protocol

4. Other Achievements

- Nothing to Report

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Nothing to report

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to report

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

1) Obtain HRPO approval to begin study
2) Execute recruitment strategy by initiating contact with veterans
3) Begin recruitment and enroll subjects
4) Collecting blood samples for genetic material testing and begin AFT, skin biopsy, sudoscan, and pupillometry testing

4. IMPACT: Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to Report

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to Report

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to Report

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to Report

5. CHANGES/PROBLEMS: The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

-Nothing to Report

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Nothing to Report

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

There were no changes in expenditures.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

- No changes to use of care of human subjects to report.
- VANJ IRB approval was granted on March 30, 2016 and an amendment to include a Research Monitor was approved on Sept 1, 2016.

Significant changes in use or care of vertebrate animals.

No animal use research will be performed to complete the Statement of Work

Significant changes in use of biohazards and/or select agents

No biohazards and/or select agents will be used to complete the Statement of Work

6. PRODUCTS: List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  Nothing to Report

  Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: Author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  Nothing to Report

Other publications, conference papers, and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to Report

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to Report

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

Nothing to Report

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to Report

- **Other Products**
  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment, and/or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:
  - *data or databases;*
  - *biospecimen collections;*
  - *audio or video products;*

- *software;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *other.*

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?
Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."

Name: Jorge Serrador, PhD
Project Role: PI
Nearest person month worked: 2
Contribution to Project: no change

Name: Kelly Brewer, MS
Project Role: Study Coordinator
Nearest person month worked: 2
Contribution to Project: no change

Name: Justyna Michalick, BS
Project Role: Research Assistant
Nearest person month worked: 1
Contribution to Project: no longer working on project

Name: Faria Sanjana, MS
Project Role: Research Assistant
Nearest person month worked: 1
Contribution to Project: Faria has been learning study procedures and compiling a recruitment list to be contacted once recruitment commences.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not

necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to Report

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.
Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Organization Name: Massachusetts General Hospital Location of Organization: Boston, MA Partner's contribution to the project: Dr. Oaklander and Dr. Klein have visited VA NJ to provide expertise in scientific protocol development and train our staff in autonomic function testing

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating PI and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to **https://ers.amedd.army.mil** for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.

9. APPENDICES: Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.